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### Global Views

# Medicine has always been "Modern" and "Scientific" from ancient times to the present day



Mikhail Teppone a,b,\*

- <sup>a</sup> Bionion Sdn Bhd, 1, Jalan Sungai Jeluh, Shah Alam, 40460, Selangor, Malaysia
- <sup>b</sup> Bhmed INC PTE. LTD., Singapore 408705, Singapore

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### ABSTRACT

Throughout human history, doctors and healers have gathered and refined the knowledge inherited from the previous generations. Different methods of effective therapy have been designed during various historical periods; when each was developed, it was considered "modern scientific medicine" for their time. Mankind has gone through natural and social disasters and survived; hence, history has proved there was no time when medical knowledge was erroneous or ineffective. Classic medicine has grown to be divided into narrow, specialized branches, causing it to lose its holistic approach and general view on health, sickness and therapeutic methods. Many of traditional medicine's effective methods have been forgotten and removed from the mainstream medicine. It would be good for modern medical education to incorporate the general knowledge of historically effective therapeutic modalities and study practical cases. Medical students should be taught how to choose a "good method" or "good medicine" independent of when that method or remedy was discovered. However, he has to keep in mind the primary goal of medicine: "I will use treatment to help the sick according to my ability and judgment..." (from Hippocratic Oath).

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### 1. Introduction

During the ancient times, similar medical theories and principles were practiced around the world despite linguistic and cultural differences. These laws and principles adhered to the concept that nature and human are united by the several basic elements, and liquids together with energy circulating within the human body and nature. This model of the nature and human body, despite its seeming simplicity, enabled various diseases to be treated using substances and methods available in the natural environment.

There is no adequate documentation of the medicinal and therapeutic practices observed by the people who occupied the Australian, American and African continents prior to the European migration to those regions.

Furthermore, there is no valid historical representation of medicinal practice in Europe before the time of Hippocrates. Only Eastern countries have retained the ancient art of healing, and

E-mail address: mikhail.teppone@gmail.com

hence have the advantage of developing it into a comprehensive medical knowledge-based system.

### 2. Traditional Chinese medicine is a unique heritage of antiquity

According to traditional Chinese medicine (TCM), energy and blood circulate through the human body using special pathways known as "channels" and "collaterals." This process supports the functions of the internal organs and protects them. When disease ensues, the cause may be internal (e.g., hereditary or strong emotions) or external (e.g., physical, chemical or biological factors) and is described by the terms "wind," "heat," "cold," "dampness" and "dryness." Some etiological factors cannot be described accurately as external or internal, and others are both nature combined.

Pathological conditions can belong to the "deficiency" or "excess" and "cold" or "hot" types. The therapeutic approaches seek to reinforce or to cleanse the body and to restore balance. Relatively simple ailments known as "outside diseases" can be treated with massage, chiropractic therapy, breathing, physical exercises, acupuncture and moxibustion. Deeper issues or "inside diseases" require additional special diet and various medications [1,2].

<sup>\*</sup> Address: Bionion Sdn Bhd, 1, Jalan Sungai Jeluh, Shah Alam, 40460, Selangor, Malaysia.

Based on their specific therapeutic effects, all herbs/medicines are described as diaphoretic, diuretic, cleansing, tonics, calming the mind, etc. Within these groups, the herbs are subdivided into hot, neutral, and cold according to their properties. In addition, herbs have various tastes (sour, bitter, sweet, spicy, salty and bland) and attitudes towards certain channels and organs. The pharmacopeia of TCM includes products of mineral, plant, animal and human origins [3].

The concept of Dao (道), unites all parts of the universe—everything known and unknown, and all connections and interactions between the parts. All parts and aspects of the universe are divided into two major groups known as Yin and Yang. Further, comparison and analysis of the relationships among the various aspects of the human body and nature are described in detail by the law of the 5 elements (wood, fire, earth, metal and water).

All these terms used in TCM first appeared in ancient oriental philosophy, and have very broad meanings in contrast to the modern scientific terms, characterized by precision and specificity. However, modern medical science has designed various mathematical models to describe the general laws of physiological and pathological processes within the human body and these models resemble the approach applied in TCM. TCM terms and principles look like algebraic equations. Therefore, these general terms enable the doctor to understand the specific condition of his patient and prescribe the correct therapeutic protocol. This is applicable not only to common diseases but also in cases of unknown etiology and pathogenesis, where modern diagnosis and treatment are undefined [4]. Ancient Indian and Tibetan medicines are similar to the TCM described above [5,6].

### 3. Modern scientific medicine in ancient Greece

The ancient Greeks' medical knowledge can be found in the Hippocratic Corpus—a collection of medical treatises written by various authors during and prior to Hippocrates's time (460–370 BC) [7]. The ancient Greeks recognized basic elements similar to those known in China and India. They described four liquids (humors) circulating within the body, including yellow bile, black bile, blood and phlegm, which have similarities to the four elements and their qualities. Four pairs of large veins described in the ancient Greek anatomy [8] were actually more similar to the "channels and collaterals" known in TCM than the blood vessels in the modern medical sense.

The ancient Greeks believed that diseases could be caused by the stagnation and accumulation of the four humors and that the body could be damaged by weather extremes, including excessive heat, cold, humidity, dryness and high winds. Further, they believed that some diseases were induced by diets rich in a certain quality (e.g., sour, bitter or salty) [9]. In order to prevent diseases and provide therapy, Hippocrates's recommendation was to follow nature—choosing a healthy place for living, wearing clothes appropriate for the weather, and consuming food and medicines which could maintain and restore the body's balance. Thus, the ancient Greeks believed that food or medicines with "dry" qualities were helpful to balance cases of dampness; "hot" food and medicines could balance "cold" conditions, and "cold" food and medicines would treat "hot" conditions.

### 4. Modern scientific medicine at the time of Avicenna

Abu Ali Ibn Sina (Avicenna, 980–1037) was a famous doctor in the Middle East [10]. At the very beginning of the first book of *Canon of Medicine*, Avicenna described the four elements as fire, air, water and earth. Moreover, he expounded on the four liquids (humors), including yellow bile, black bile, blood and phlegm, which circulated within the human body. Avicenna also went on

to explain the various conditions of the human body—warm, cold, dry and humid and that the energy of the body could be in excess, deficiency or balance.

Besides his detailed description of the arteries and veins, Avicenna identified "energies" or "living forces" and their relationships to the organs. Among the etiological factors for disease, Avicenna noted various types of weather that were related to the seasons. Moreover, he advised that special attention should be paid to the wind that blew from certain directions. He concluded that some diseases were caused by living conditions, emotions, sleep quality, nature or the taste of food and beverages. Avicenna had deep understanding of different diagnostic methods which resemble the methods used in TCM, including analysis of pulse, urine and stool [10].

The *Canon of Medicine*, written by Avicenna, is a collection of medical knowledge from the Far East, Middle East and Europe, particularly from Greece, which was the reason why Avicenna's books were used in Europe as a medical canon by doctors for generations [11].

# 5. Great turn in the medical paradigm at the time of Dr. Paracelsus

For centuries, there was only gradual change in medical knowledge. In every generation, doctors improved on the knowledge that they had inherited from the previous generations. For research and everyday practice, doctors still referred to classic books written decades and centuries previously because human's medical needs had changed very little over the intervening centuries. Crucial changes in medicine began with the development of the various fields of science. These changes are linked to famous historical discoveries and names.

Philippus Aureolus Theophrastus Bombastus von Hohenheim (1493–1541), one of the famous doctors in Medieval Europe, was born in Switzerland. Like all learned people of that time, he was an astrologist, alchemist, philosopher, magician and a medical doctor. Philippus was known as a "reformer" in medicine, and at times, was compared to Martin Luther, who was a reformer in religion. Therefore, he was called "Luther in medicine" [12]. But Philippus's attitude towards medicine was different from other doctors. He recommended rejecting all knowledge of the past so that he could build a new perspective for medicine based on his own experience. Hence, he was more of a hero of revolution rather than reformation [13].

In a medical school, Philippus studied books written by ancient authors. However, prior to his first lecture at the University, he publicly burned commonly used medical textbooks, including the works of Avicenna, Galen, and others, saying, "Sic vos ardebitis in gehenna," which means "It will burn in hell" [12]. One could assume that either Philippus did not understand the medical principles described by his great predecessors or he considered that his own knowledge and experience were sufficient for the future development of medicine, and hence he did not see the need of medical sciences from previous centuries. He even took a nickname "Paracelsus" that literally means "beside" Celsus or "greater than Celsus" [13].

"Paracelsus" rejected the liquid theory related to the human body. He reckoned that diseases were caused by chemical changes within the body so the therapy should be based on chemical substances that could fix abnormal chemical conditions. For Paracelsus, he considered mercury and antimony as primary medicines. However, he also used medicines derived from plants, and opium was one of the most popular ingredients in his pharmacopeia [12].

The new trend in medicine, then, was to differentiate diseases based on chemical changes, and to find or design a pure therapeutic substance which could reverse the chemical changes related to each specific disease. The implementation of this approach was impeded by the lack of essential diagnostic technology during the time of Paracelsus. Biochemical tests of animals and human tissues became available only at the beginning of the 19th century [14]. The first publications dealing with hematological tests appeared at the end of the 19th century [15]. The first demonstration of X-ray imaging took place only in 1895 [16]. The first case of ultrasound diagnostic was published in the middle of the 20th century [17].

Nevertheless, the great revolution in the medical paradigm started at the time of Dr. Paracelsus and continued on for centuries. Gradually, classical medicine lost its holistic and systemic approach and was replaced by increasing specificity: specific names for diseases, types of pathogenesis, specializations in the narrow fields of the healthcare and specific medicines to restore certain chemical changes. Concurrently, the concept of a "prominent doctor" was replaced by the "efficacy of the chemical substances."

# 6. Chemically based medicine with the precise choice of the chemical substance

Another trend that emerged from the evolution of medicine can be traced to Samuel Hahnemann (1755–1843), the founder of homeopathy. Through his theory and experiments, Samuel Hahnemann concluded that a "poison" that caused certain symptoms in the body, known as its "pathogenesis," could be used to treat these particular symptoms when given to the patient in a tiny dose. Homeopathic "therapeutic poisons" are from the natural environment, for instance, toxic substances from minerals, plants and animals

The homeopathic pharmacopeia was a collection of remedies from the historical records of poisoning supplemented with results from animal experiments and human clinical trials. The efficacy of homeopathic treatment was believed to depend on the similarity between the symptoms of the disease and the pathogenesis of the substance used [18–20].

The Principle of Similarity is presented in the homeopathy by the specific pathogenesis of the remedy, by the individual features of the patient and by the specific clinical manifestation of a disease. For example, if the main symptom is pain, various characteristics of the pain would be analyzed, such as location of the pain, the predominant side of the body affected by the pain, the usual time the pain occurs and subsides, factors that strengthen and weaken the pain and even secondary symptoms associated with the pain. Homeopathic treatment is effective only in cases of individualized prescription, which must be adjusted constantly as the patient's symptoms change [18–20].

It takes a knowledgeable and an experienced physician to be an expert in homeopathy since he has to remember a vast number of "pathogeneses" with their specific symptoms and additional modalities. Furthermore, he must be able to differentiate between the various "pathogeneses" with similar symptoms in his search for the one that best matches the patient's clinical manifestation of the disease.

If a researcher conducting homeopathic clinical trials does not have sufficient knowledge and experience in this particular field, he will not be able to obtain good results from the study, and thus will conclude that the homeopathic therapy did not work. An unqualified researcher may even present the results from the clinical trials as a modern statistically proven paper to affirm that homeopathy is, indeed, ineffective.

Homeopathy, psychotherapy, chiropractic, acupuncture, massage and even surgery fall under the realm of healthcare where the effectiveness of the therapy relies mainly on the qualification and experience of the practitioner rather than on the tool (e.g.,

lancet, acupuncture needle, massage oil and medicines) of the healer.

### 7. Organ-specific remedies throughout the centuries

The concept of using "organ-specific remedies" to treat diseased organs was quite common among ancient doctors. Berridge [21] wrote that principle *similia similibus curantur* or "like cures like" as a rational empiric mode of treatment was already known in Europe at least in the 12th century. In the 16th century, German Magician Heinrich Cornelius Agrippa (1486–1535) expressed a common view of his time: "As it is WELL KNOWN amongst physicians that brain helps the brain, and lungs the lungs" [22].

A detailed description of how to use parts of different animals to cure various diseases could be found in the *Natural History of Pliny the Elder* (AD 23–79), written in the first century AD [23]. This unique document also confirmed that goat and sheep placenta had already been used by physicians in treating female disorders [24].

In 1498, the officials from the guild of doctors and apothecaries in Florence published the European pharmacopoeia *Ricettario Fiorentino*. It included a list of prescriptions that apothecaries were bound by law to follow. Simple ingredients and complex prescriptions were drawn from the books of Dioscorides, Serapio, Galen, Rhazes, Avicenna and other famous physicians prior to and during that era [25]. Its 1789 edition comprised various animal-derived remedies, for example, deer antlers, lobster gills, cuttlefish bones, fat of duck, or rabbit, or bear, and also various types of insects, including Spanish flies, cochineal and ants [26].

The first edition of the *Pharmacopoeia*, complied by Johann Schroeder, was published in 1641. Tinctures or extracts were made from the spleen of bull; from the heart of wolf; from the liver of wolf, frog or pig; from the lungs of sheep, pig, bear or fox; and from the bone marrow of cow, horse, dog or sheep. Deer placenta and human placenta and umbilical cord also were included in the list of the simple ingredients of therapeutic remedies [27].

Discoveries by Giovanni Battista Morgagni (1682–1771), who established the anatomic concept of diseases originating from organs [28,29], reinforced support for the "organ-specific remedies." Since that time, doctors could ignore the essential relationship between a symptom and its related organ, but could diagnose the location of the problem quite precisely. As a result of that discovery, doctors could use specific parts from the animals to treat the corresponding organs and tissues in human.

# 8. Application of animal tissues and organs for replacement therapy

The first attempt to use animal origin products for injection, transfusion or even in a surgical transplantation was reported in the 17th century. In 1667, the earliest cases of blood transfusion from sheep to human were reported in France [30] and in England [31]. In 1668, a Dutch surgeon J. van Meek'ren cited a case from Russia where dog bone was grafted into a patient's skull [32]. Yet surgical transplantation of animal tissue into the human became a common medical practice only two centuries later.

A new dictionary of practical medicine and surgery, published in 1872, had already described successful transplantation of skin taken from guinea pig, dog or rabbit [33]. Further, a piece of mucous membrane from a dog was successfully grafted into the mouth of a boy in the case of spurious ankylosis of jaws [34]. Two cases involving dog bone transplantation to close the defect of a patient's skull were reported from England [35] and France [36].

In addition, Dr. Helferich, of Munich, transplanted a muscle from dog to a female patient to refill the gap left by removal of a large fibrosarcoma (1882) [37]. Dr. Gersung of Vienna, an assistant to Prof. Billroth, performed successful transplantation of a sciatic nerve from a rabbit to a patient who was a professor of the university, Dr. Ernst von Fleischl (1885) [38]. Thyroid gland transplantation from sheep to a patient with myxedema was performed in 1890 [39].

In 1890, Dr. Themistocles Gluck was of the opinion that cellular therapy was slowly yet steadily developing, based on the theory of cellular pathology; positive results in various types of transplantation expressed the cellular therapeutic direction in its purest form [40]. However, all the examples mentioned above are related to replacement therapy, where the defects of a certain organ or tissue were substituted with similar tissue from animals, which was only a part of the concept of cellular therapy in the general sense.

## 9. Cellular therapy designed by Dr. Charles-Édouard Brown-Séquard

Organ-specific products from animals were being used in the classic medicine even during the mid-19th century. In 1857, a special chapter "Animals Yielding Products Employed in Medicine" was included in the Supplement to the Pharmacopeia, published in London. It detailed the general descriptions of various animals, as well as indications and prescriptions of animal-based remedies compiled from medical books of the past centuries [41].

A new step in the development of modern medicine followed the work of Rudolf Virchow who declared in 1855 that disease was pathology of cells [42,43]. That theory was foundational to our contemporary understanding of pathogenesis of diseases, and it also encouraged development of a new field in the medicine, known later as the stimulating or rejuvenating type of cellular therapy.

At the end of 1860s, during a series of lectures at the Faculty of Medicine in Paris, Dr. Charles-Édouard Brown-Séquard explained that some organs, particularly the glands, had specific influence on the nervous centers. He also proposed a new idea of intercellular interaction: "if into a man, old or feeble, the living cells of a young and vigorous being could be injected, why should he not vibrate in unison with this fresh life, which pervades him so intimately [44]?"

During the 1870s, Dr. Brown-Séquard and Dr. D'Arsonval carried out the experiments of grafting endocrine glands between animals. Later they prepared extracts from the different glands of donor animals and injected them into experimental recipient animals [45].

From the very beginning, research and development of cellular therapy—as a stimulating or rejuvenating method—were divided in two different directions that sometimes overlapped. However, in several decades, both of them were partly replaced by therapy that relied on hormonal remedies. Doctors from one group used extracts from organs of animal, but another group of doctors preferred to use whole living organs, or pieces of the tissue taken from animals.

# 9.1. Rejuvenation cellular therapy with the extracts prepared from animal origin tissue

In 1889, Dr. Brown-Séquard presented his own clinical trial whereby he injected himself with testicular extract derived from young dogs and noticed that his condition had improved tremendously, including general physical strength, brain function and even urination and defecation [45,46]. We can assume that Dr. Brown-Séquard had low testosterone level, and it was increased after injection of extracts from dog's testicles. But according to the modern study contents of testosterone in the injected liquid were not enough for therapeutic effect [47], so it was not replace-

ment therapy in the modern sense. Actually, it was a new version of the stimulation and rejuvenation cellular therapy, based on the old principle which was to use organ of the animal to treat the same organ in the human.

Soon after, Dr. Variot reportedly injected his patients with fresh testicular extracts derived from rabbits or guinea pigs, with similar optimistic results [48].

Obvious rejuvenation in the experiments on animals, and similar effects among patients who were injected with extract derived from testicles of guinea pigs, but were not informed about the contents of the liquids or their expected effects, helped to dispel the notion that positive results were due to the power of suggestion.

In 1891–1892, Drs. George Murray and Wallace Beatty presented several cases where myxedema had been cured successfully with liquid obtained from sheep's thyroid glands [49–51]. In 1894, Dr. Derrien also published a short review of myxedema being treated using extracts derived from the thyroid gland, and he argued that, although the mode of action was only hypothetical, the action itself was unquestionable [52]. Similar technology was used to treat various syndromes related to diseases of ovary and uterus or to premature menopause [53]. This therapy of applying extracts from animal organs became known as the "Brown-Séquard method" [54–55]. The treatment by the injection of goat lymph mixed with extracts derived from goat brain and testicles known as the *Roberts Lymph Treatment*, was one of the versions of animal-derived "cellular therapy" [56].

The book *System of Practical Surgery*, published in 1904, has a section focused on treating tetany and cachexia after excision of the thyroid gland. The author commented, "Organotherapy has been very successful, whereas other methods of treatment have been devoid of results. Transplantation of the thyroid gland, or injection with thyroid (*extract*), or internal administration of thyroid gland tissue has been followed by brilliant cures" [57].

In the early 20th century, organotherapy was already known as a scientifically based and effective therapeutic method. Efficacy of organotherapy depended largely on the work or multiple professionals, including the pathologists who traced relation of the symptoms to the sickness of certain organs, the physicians who discovered similar symptoms in the patient and the chemists who handled with the animal organs, extracting their chemical components, and transforming them into forms which could be administered to a patient [58].

# 9.2. Therapeutic and rejuvenation cellular therapy by the transplantation of whole glands

After the successful case of testicle extract injections reported by Dr. Brown-Séquard [45], surgeons in Europe started transplanting sheep thyroid glands into patients suffering from myxedema [39,59,60]. Almost 25 years later, Dr. Voronoff presented a case where a boy with myxedema received both thyroid and parathyroid transplants. The uniqueness of this case was that the thyroid gland was taken from an ape [61] and that four years later that patient "had been declared ... fit for military service and had marched to defend his country like any other man" [62].

The next transplanted organ was a testicle. There were some discussions on the priority of a case where an animal testicle was grafted into a human, but now it is clear that Greek surgeon Skevos Zervos was the first to perform the transplantation of ape testicle to a man in 1910 [63]. Twelve years later, Max Thorek analyzed the results of similar transplantations and proved histologically that testicles taken from apes and transplanted to men were vascularised and in full activity [64].

#### 9.3. Fusion or combination of both types of cellular therapy

At the close of the 19th century, doctors had already developed therapy in the case of hormone insufficiency. The technique used was either grafting the corresponding organ [39] or injecting fresh or preserved extracts prepared from the counterpart organ of the donor animal [45].

In 1892, Italian Prof. Capparelli [65] presented results of experimental transplantation of small pieces of pancreatic tissue, not by conventional surgery, but simple injection by syringe. Twenty years later, Dr. Hermann Küttner shared his experience on curing thyroid gland insufficiency. He stated that, up to that point, endocrine gland transplantation had not produced a permanent result the implanted organ usually degenerated and eventually might undergo necrosis and absorption. Thus, Dr. Küttner [66] suggested that thyroid gland implantation should be followed by injection of thyroid tissue emulsion. More than a decade later, in 1927, Drs. Kurtzahn and Hübener [67] reported immediate physical and mental improvement using Dr. Hermann Küttner's method in two out of three patients with myxedematous cretinism. Drs. Kurtzahn and Hübener treated their patients by injecting 4-5 mL of fresh thyroid tissue pulp intramuscularly. Although the results were not long-lasting, the procedure had the advantage of being easily repeated. In 1929, Dr. Küttner once again attracted the attention of other physicians when he performed an endocrine gland tissue transplantation by injection. This method had its benefit, as the procedure was only a minor surgery, done under local anesthesia, and could be repeated as soon as the effect of the treatment diminished [68,69].

Meanwhile in 1931, Dr. Paul Niehans, from Switzerland, injected a suspension containing small pieces of parathyroid gland tissue, taken from a newborn ox, into a female patient with tetany, caused by an accidental surgical removal of her parathyroid gland. The effect was a total miracle—all her symptoms disappeared. She went on to live for more than 30 years and died at the ripe old age of 94 [70.71].

Subsequently, injections of diluted dried cells and small pieces of live animal tissue gained popularity as treatment for delayed development in childhood [72–74], and in anti-aging and rejuvenation programs [75,76]. Improvement in the objective and subjective parameters in a clinical trial comprising a large group of children with Down syndrome [77] rejected the hypothesis of "placebo effect" as the mechanism of the therapy.

# 9.4. Organ-specific cell therapy was supplanted by hormonal replacement therapy

By the beginning of the 20th century, physicians and physiologists had already gained understanding of the internal secretions made by ductless glands. The first chemical messenger that regulates digestion (secretin) was discovered by William Bayliss and Ernest Starling in 1902 [78]. In 1905, the new term "hormone" was presented to the medical world [79–81]. Over time, in addition to the transplantation of entire endocrine glands, suspensions of live cells and extracts of organs, physicians devised a new method of replacement therapy, using pure hormones extracted from animal organs or synthesized biochemically.

Due to the active and effective application of hormonal remedies, the popularity of cell therapy gradually declined. Only a small group of experts in cellular therapy, mainly in Germany, France, Switzerland and Russia, continued to use live cells or cell extracts as a part of their daily practice. The leading argument suggested by those doctors was that cell therapy was not limited by the effects of hormones, and it could include substances not yet identified. But science was advancing and now, recent studies have identified

peptides that are specific for various organs and can contribute to recovery of the specific organ [82–84].

Besides, some of the degenerative diseases of internal organs, brain, peripheral nerves, muscles and other tissues are not caused by hormonal deficiency, thus hormonal therapy would not be effective. Therefore, this small group of "incurable" diseases and syndromes could be a niche for further research and practical application of cellular therapy.

# 10. Further development of chemically based scientific medicine

At the close of the 18th century, Dr. John Brown (and G. Cullen) believed that all pathological and healthy conditions could be classified as *sthenic* (active) and *asthenic* (nonactive) diseases respectively, with the normal condition in-between. *Sthenic* disease could transform into *asthenic*, and vice versa. They used stimulating or sedating therapy, including tonic remedies and warming methods or cleansing and bloodletting, according to the activity of pathological process and patient's body status [85]. During the 1930s, Dr. Hans Selye reconfirmed the dynamic changes in pathological conditions from the alarming phase (*sthenic*) to exhaustion (*asthenic*) and described that transformation by applying the general adaptation syndrome theory [86,87].

As mentioned before, ever since the time of Paracelsus, there was a widespread desire to study chemical changes, especially for certain diseases. Achievements in medicine went hand-in-hand with the development of diagnostic equipment. Various active "chemical substances," which play an important role in the animal and human body, were discovered, including proteins, lipids, carbohydrates, minerals (before the 20th century), hormones (1902) [78–81], the kinin-kallikrein system (1909) [88], vitamins (1910–1912) [89], prostaglandins (1935) [90], free radicals and antioxidants (1954) [91,92] and endorphins (1975) [93].

Stimulating methods and replacement medicines are usually recommended for cases where low-functioning activity or "insufficiency" (asthenic condition) occurs. Application of active substances, such as hormones, vitamins, blood, or bone marrow, serves as a common replacement therapy. On the other hand, when the functional activities of certain organs, tissues, cells (tumor or bacteria cells) or ion pumps are unreasonably high (sthenic condition), the modern treatment is to apply blockers, inhibitors, antagonists or even surgery. This involves medicines such as β-blockers, H<sub>2</sub>-blockers, prostaglandin antagonists, antihistamine medicines, calcium pump inhibitors, cytostatics or antibiotics. As an example, following the discussion of "sthenic" and "asthenic" types of diseases, phosphodiesterase type 5 (PDF-5) inhibitors would be a logical choice only when there is a high activity of PDF-5, for instance in the case of diabetes mellitus patients [94], but not in the case of erectile dysfunction with normal or low activity of PDF-5. All treatments using inhibitors, blockers or antagonists should follow this approach.

# 11. Main obstacles to the development of today's modern scientific medicine

An assumption can be made that the factors limiting the development of modern medicine are rooted in how a medical doctor is educated. The process of training a medical doctor is very different than the training given in other natural sciences or the arts. For example, a child learns to count in the first years of his life. He starts by counting with his fingers, gradually moves on to more complex calculations, and he puts this knowledge to daily use. At the university, he studied about the most advanced type of

calculation during that time. This process of education actually replicates the historical development of mathematical science. The same is true about physics, fine arts or music.

Education in the field of healthcare is quite different. Medical science begins with the usual familiarity of vaccinations and pills for headache or common cold. At school, the basic knowledge in biology is imparted to the students. Then, at the university, a medical student is proficient solely in the latest achievements of medical science and practical experience, but he has very little knowledge about therapeutic methods and medicines from thousands or even hundreds of years ago.

Up till the Middle Ages, the gradual progress of medical science was tied to the achievements of its many prominent practitioners. Subsequently, the new knowledge resulted in the revolutionary development of the basic sciences, including physics, biology and chemistry, causing radical advancement in the fields of physiology, pathology and pharmacology.

Since the time of Dr. Paracelsus, classic medicine has seen continuous sweeping changes. Describing this progression, Dr. William C. Krauss commented in 1893, "The epoch in which we live may well be called the sky-rocket period of the 19th century. Men, like methods, approach their zenith with an increasing roar and sparkling brilliancy, and as suddenly fade, to fall with dull and heavy thud. What was yesterday a seemingly brilliant success becomes today a glittering failure, and the shores of time are laden with the wrecks of 'wonderful discoveries'" [95].

Due to the strictly regulated medical practices, many aspects of the ancient medical science are forgotten or their use is forbidden. Thus, a "well trained doctor" mainly means that the physician is knowledgeable in the findings of modern research but is uninformed of the vast medical experiences from the past generations.

During their graduate education, some doctors would like to fill in gaps in knowledge between contemporary and ancient or medieval medicine, but differences in the terms used in the ancient and modern medical languages make it difficult. Moreover, the medical community has forgotten that throughout human history doctors have practiced the most "modern scientific medicine" of the time. Now these older versions of modern medicine are called "folk" or "alternative" medicine, and the lack of knowledge about the achievements of previous generations has led to a skeptical attitude toward the medical experience of the ancient physicians.

Another obstacle lies in the manner of how diseases are classified. Although classification basically uses the general parameter to describe the localization of the pathological process, the succeeding steps are not systematic and are unnatural. Some diseases are titled and categorized based on their macro- or microstructural changes, including cytological or histological findings, but others are described by the various functional abnormalities detected by instrumental examination (e.g., blood pressure measurement, electrocardiography and electroencephalography) or by laboratory tests (e.g., blood or urine analyses), etc. Further, there are some diagnoses that have no scientific definition and do not fit into the concept of modern diagnosis at all. These include "chronic fatigue syndrome," "irritable bowel syndrome," "restless legs syndrome," "ingrown nails," "hyperactive child," "acrophobia" and "claustrophobia," among others.

Classification sets back the organizing of homogeneous trials and control groups because patients with a similar nosological form may be grouped together but may not have the same clinical manifestations or the same internal abnormalities, as verified by modern diagnostic analysis. Usually, patients in a group share only the main parameters described by the identification of the nosological form. For example, in a group of duodenum peptic ulcer patients, there were at least 4 different subgroups, as identified

by the complaints and clinical manifestations which required different therapeutic protocols and had different treatment durations [96].

The modern trend is to define the chemical changes in each nosological form or pathogenic mechanism and to develop pure medicines with specific effects for the particular pathogenic mechanism or disease. Hence, any secondary or additional effects of the medicines are regarded as side effects. If a patient suffers from several nosologic forms bearing different chemical changes, he would require more than one type of medicine to address each malady separately. This causes polypragmasia, unnecessary prescription of multiple drugs, to be fairly common in contemporary medical practice.

In the modern pharmaceutical world, studies described as "double-blind trials" are far from perfect. This kind of study can be applied only to a specific group of medicines with relatively short therapeutic effects depending on the dose. But there are no clinical trials for the standard "inert" substances used as the "placebo." There are no trials to compare the efficacy of the different "inert" substances in treating various diseases. There is a common belief that either the "inert" substance itself possesses no pharmaceutical activity within the patient's body or its effect is negligible. But in TCM, "inert" substances, like powder of gypsum, have been used successfully for centuries for treating ailment with hyperproduction of heat described as "heat" or "fire" diseases [3], and seashell powder was used to treat mental disorders [3].

Even glucose solution can be an effective remedy. It can be used to alleviate slight hypoglycemia in order to avoid related health problems. Understanding this pathogenic mechanism led to use of glucose solution to treat bronchial asthma effectively before corticoid hormones were available [97–99] which is still practiced [100].

In general, without clinical trials for the "inert" substances used in the placebo there is no basic benchmark for other clinical studies, comparisons and scientific conclusions.

The attempts to carry out randomized, blinded, sham-controlled trials of acupuncture [101] or surgery [102] demonstrate adherence to modern requirements, with little or no understanding of the techniques and mechanisms that produce the therapeutic effects for these micro- and macrosurgical modalities.

Some odd findings have shown similar efficacy in sham and real surgery groups, thus further research and debate on the issue are required; one question is whether all "surgical diseases" actually need surgical treatment or whether some surgical cases can be cured by nonsurgical methods [103,104].

Interestingly in the current version of "modern medicine," any unknown therapeutic mechanism is commonly explained using the "placebo effect theory." This does not clarify the therapeutic mechanism, but it provides a safe way of saying "I don't know how it works."

### 12. Integration of tradition with modern scientific medicine

To improve healthcare, medical education should be the starting point. Along the path to becoming a doctor, medical students should be made of all the scientific medical modalities that have been applied throughout the generations—in theory and practice. The education should then be finished with the most recent achievements in the field of medical science.

Modern categorization of diseases should be developed into a systemic classification with the important labels like "sthenic" (excess) or "asthenic" (deficiency) and "hot" or "cold." This additional information is easily recognizable after a routine observation and examination of the patient. For example, expiratory dyspnea, or cough, during deep inhalation indicates "excess in the lungs"

(sthenic), while inspiratory dyspnea, or cough during exhalation, indicates "deficiency in the lungs" (asthenic). Experiencing abdominal pain on empty stomach is an indicator of "deficiency of the stomach" (asthenic), whereas having abdominal pain after a meal indicates an "excess of the stomach" (sthenic). Excess and deficiency should require different therapeutic protocols.

Characteristics of diseases related to "hot" and "cold" syndromes can be easily recognized from the analysis of the patient's avoidance or preference for the "cold" and "hot" patterns, for example, inclination to cold or hot weather, certain types of food and beverage choices, or fondness for warm or light clothing.

It is highly desirable to develop simple protocols and equipment that can obtain objective criteria from these subjective signs. For instance, the ratio between heart rate and respiration can differentiate hot (> 5) or cold (< 5) syndromes [105]; and the duration of the "individual minute" can help to evaluate the adaptation or conservation of energy in the body [106–108].

It would be beneficial to find a scientific explanation for these universal patterns, which may be related to tissue respiration, contents of adenosine triphosphate and efficacy of its usage. But, even without this additional knowledge, doctors can still treat known or even unknown diseases and syndromes using "stimulation" or "sedation," "warming" or "cooling" methods or medicines accordingly.

The research protocols in modern pharmaceutical trials are too simplified, resulting in the inability to detect the therapeutic effects of the different methods and medicines used throughout the centuries [109–111]. To overcome this issue, various protocols of clinical trials should be developed for pure and complex medicines as well as pharmacological and nonpharmacological therapeutic modalities.

A doctor supervising a clinical trial pertaining to a specific field in medicine ought to have sufficient knowledge and practical experience in that field. If a researcher carries out a study in a field that is new to him, and obtains "negative results," they should be accepted as "valid results" only if the researcher has previous publications dealing with the same therapeutic modality with "positive results." Otherwise the lack of knowledge and inappropriate research protocol can cause clinical trials to result in negative conclusions. One cannot imagine that a novice surgeon would publish a first article reporting negative clinical cases, but it is quite common that a beginner published results reporting no efficacy of acupuncture, homeopathy or cellular therapy. Unfortunately in the medical community the insufficient experience of the researcher is not taken into account in regard to his unsuccessful clinical trial if study has been done according to the modern pharmaceutical standard.

During pharmaceutical clinical trials, it would be advantageous if descriptions of modern medicines include additional information on their "hot" and "cold" qualities, aside from their primary and secondary therapeutic effects. Describing medicines using their "hot" and "cold" qualities enables individualization of therapy, which decreases the risk of side effects even when various medicines and therapeutic modalities are utilized simultaneously. This was a common and compulsory practice during ancient times till the Middle Ages. The following two protocols exemplify this approach rather well:

In TCM, there is a group of antipyretic herbs which are prescribed according to the patient's symptoms: (1) initial fever with general cold feelings—Herba Ephedrae is recommended; (2) initial fever with general hot feelings—Folium Mori Albae or Herba Menthae Haplocalycis; (3) initial fever with intensive sweating or tension in the muscles—Ramulus Cinnamomi Cassiae; and (4) fever with alternating cold and hot feelings—Radix Bupleuri [3]. But in the case of severe feverish illness with various types of bleeding, or skin rashes—Radix of Isatis tinctoria should be applied [3].

Another example is the application of acetylsalicylic acid (aspirin), which is one of the ingredients in modern antipyretic pills. The natural source of aspirin is found in the cortex of the willow tree (Salix alba), known in TCM as Liu Shu Pi. The primary roles of Liu Shu Pi are to "cleanse the heat" and "promote the Yin" [112]. Thus, the consumption of Liu Shu Pi in the form of pills or decoction increases tolerance to external heat (hot weather, hot food or hot beverage) and reduces production of internal heat (exothermic chemical reactions). Based on this brief description, a TCM expert knows that only "hot" syndromes or inflammations resulted from the pathogenic "heat" should be treated with aspirin. Therefore, it is logical to use aspirin to prevent blood clot caused by the "blood stasis" due to the "heat." But aspirin should not be applied in most cases of rheumatoid arthritis with the symptoms of "cold" combined with "wind" and "dampness," or in cases of "cold" types of bronchial asthma, known as "aspirin asthma,"

The above examples demonstrate the possibility of treatment based on common subjective symptoms. Deeper study of TCM allows the doctor to learn and understand the valuable medical knowledge used throughout the centuries.

Today, physicians can easily find logical modern explanations of ancient terms and theories [4,113,114]. Hence, a doctor, trained in classic modern education, can broaden his view on the therapy by studying the various fields in the art of natural healing. Just like studying foreign languages can help to gain more information, adding knowledge of "alternative" medicine to conventional medical science can expand the possibility of gaining insight related to the diagnosis, prophylaxis and treatment. It is known that in some mathematical equations, experts even use "imaginary unit" (i), which does not exist in nature, to find answers in cases of "unsolved" mathematical problems. Similarly, doctors can use terms and theories from ancient medical systems as a mathematical model to find a therapeutic protocol, even in the case of an unknown or incurable disease or syndrome.

For example, the TCM theory of channels and collaterals describes hidden relations between the internal organs and bones, muscles, fingers and toes, skin regions, zones on the tongue, and a certain area of the radial artery. So, a localized itch on the skin, ingrown nail, or creaking in the joints points to a related internal problem, thus allowing the physician to prescribe an effective therapy. In some cases, the location of the symptom could be quite a distance from where the problem started and the areas recommended for therapy [115,116]. Without this knowledge, even an experienced physician may observe the various symptoms throughout the body but not observe the connections and relations among them.

## 13. Conclusion

Throughout human history, prior to the Middle Ages, doctors and healers gathered and refined the knowledge inherited from previous generations. This growing practice was always considered the "classic modern scientific medicine" of the time. Despite natural and social disasters, mankind has survived until today, with its population in the rise—an evidence that at no time when medical knowledge was wrong or ineffective.

One can argue that various wild animals also survived even without healthcare, but actually they use their own primitive type of medicine [117] and their surviving depends mostly on the human expansion [118].

It is rationally acceptable for a physician to comply with the standard protocols of therapy immediately after graduating from medical school. As time progresses, a physician should become an expert using his own unique professional experience. He should become a "good doctor" who knows how to choose a "good

method" or "good medicine" in specific cases, regardless of when that method or remedy was discovered. If it is a common cold or flu, a prescription of herbal tea may be sufficient [3]. For treatment of acrophobia, homeopathic *Argentum Nitricum* is one of the best choices [119]. The restless legs syndrome should be treated by acupuncture and herbal medicine [1,120]. For bronchial asthma attack, infusion of glucose solution could be quite effective [97–100]. But in the case of organ failure, hormone therapy [78–81] or transplantation of cells, tissue, or even the whole organ may be required [39,46,63].

A modern physician should remember that the primary goal of medicine has always been the same, now and a thousand years ago: "I will use treatment to help the sick according to my ability and judgment ..." (from Hippocratic Oath).

#### **Conflict of interest**

The author declares that he has no competing interests.

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